EXHIBIT 87

An Overview of Medications Utilized in Cancer Pain Management

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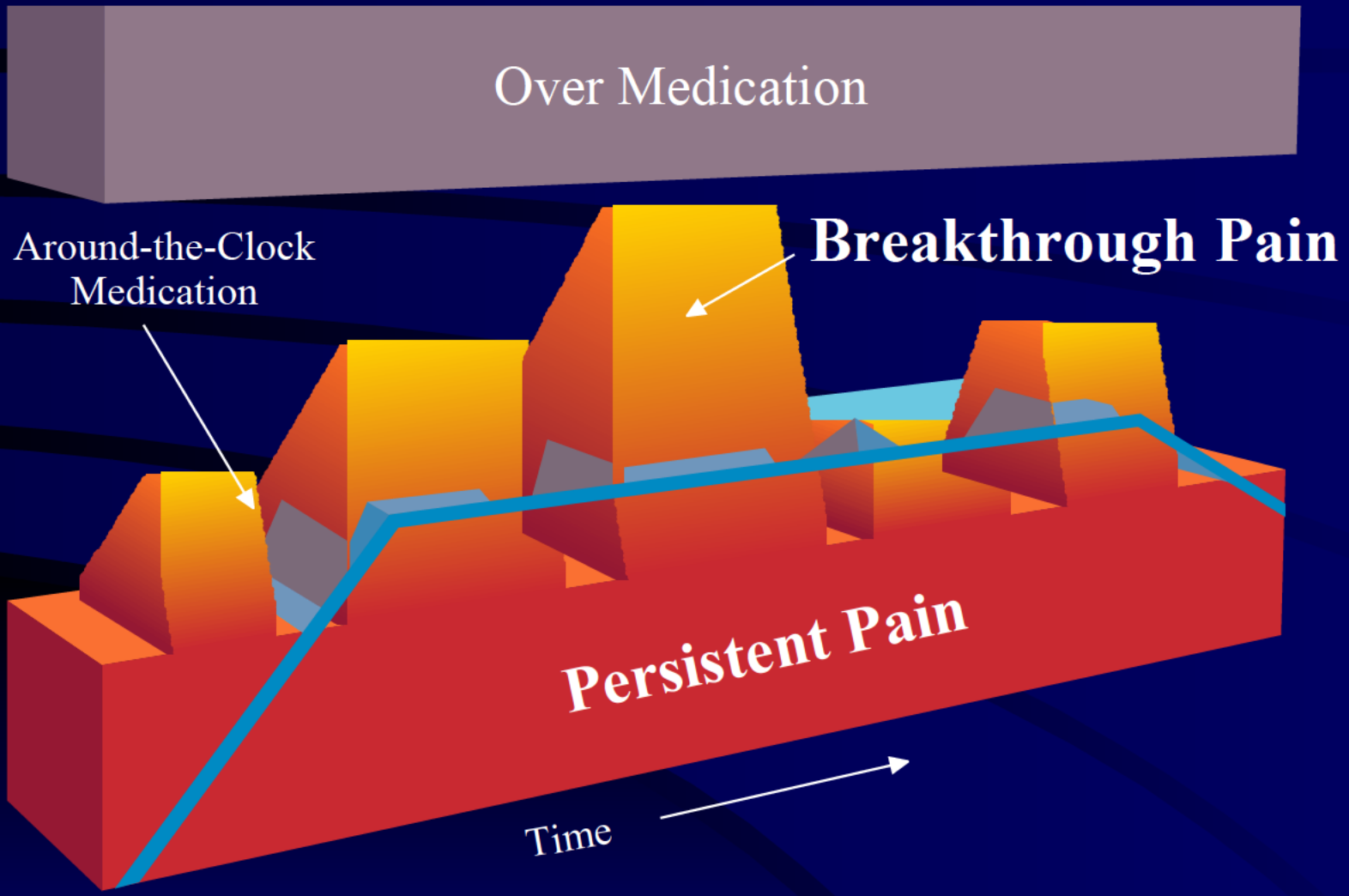
Chronic Malignant Pain

- Combination of acute, intermittent or constant components.
- Can lead to anxiety, depression and insomnia.
- Inadequately treated pain can become progressively more severe and cause relentless suffering.
- Can accelerate the patient's physical and psychological condition.

Two Components of Chronic Pain



Persistent vs. Acute Pain

Persistent Pain

- Constant or continuous pain of long duration
- "Basal or baseline pain"
- Experienced 12 or more hours per day

Acute Pain

- Sudden onset (i.e. pain due to CA bone mets)
- Can be "pain emergency"

Breakthrough Pain

- Transitory episodes or flares of moderate to severe pain occurring in conjunction with chronic persistent pain that is otherwise controlled.

Prevalence of Breakthrough Pain

- 52-64% of inpatients referred to cancer pain service
  - Memorial Sloan-Kettering surveys
- 67% of outpatients in multi-national study
  - IASP Task Force on Cancer Pain
- 86-89% of hospice patients
  - US outpatient survey
  - UK prospective inpatient survey

From: Portenoy RK. *Pain* 1990;41:273-281. Portenoy RK. Symposium on Breakthrough Pain, 15th Annual Scientific Meeting of the American Pain Society, November 14-17, 1996, Washington DC.
Caraceni A. *Pain* 1999 Sep;82(3):263-74
Fine PGJ Pain Symptom Manage 1998 Sep;16(3):179-83
Zeppetella GJ Pain Symptom Manage 2000 Aug;20(2):87-92

Characteristics of Breakthrough Pain

- Rapid onset (<3 minutes in 43% of patients)
  - May also have a gradual onset
- Moderate to severe intensity
  - Often extreme, immobilizing the patient and causing severe distress
- Relatively short duration
  - Mean duration 30 minutes (range 1 minute to several hours)

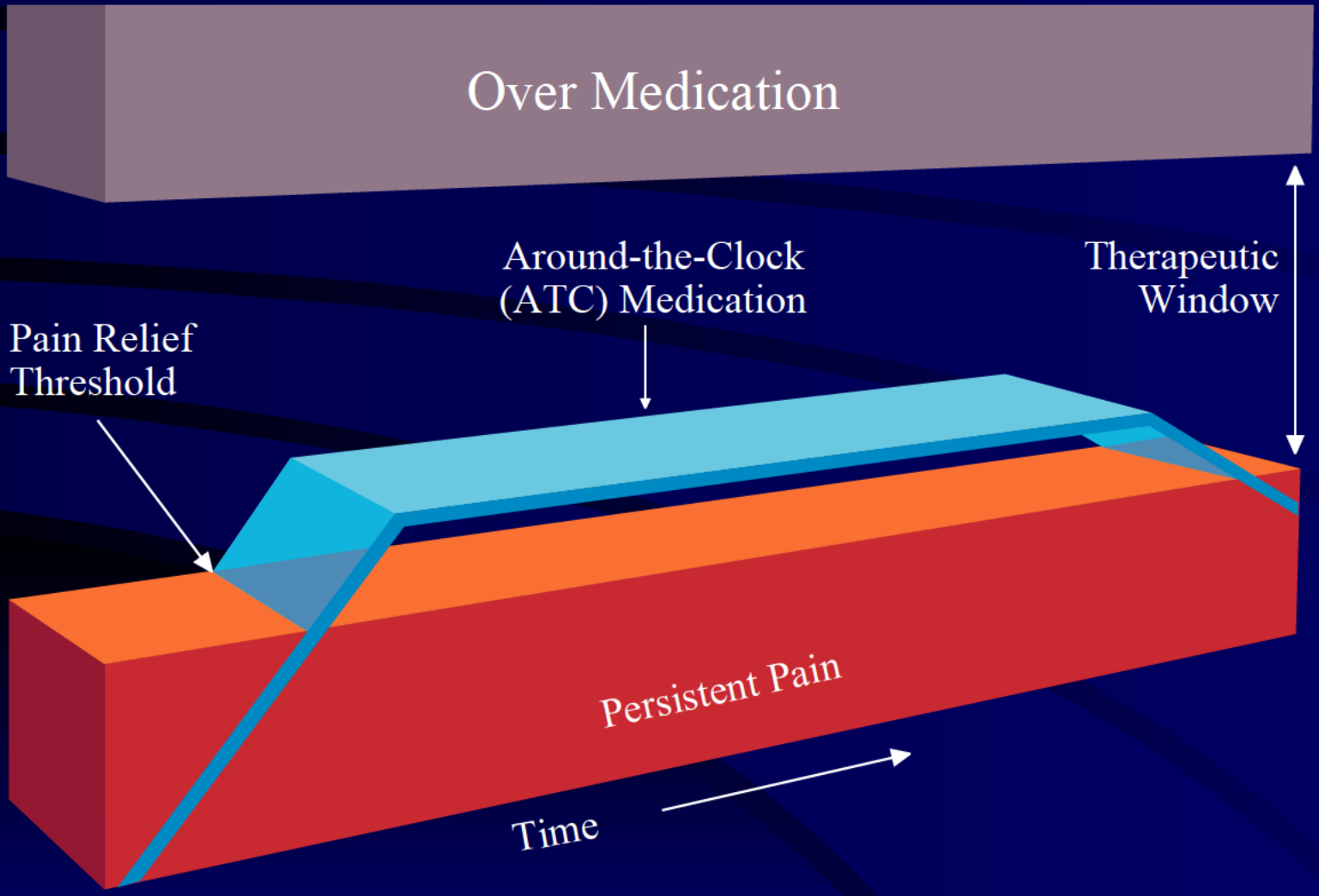
Characteristics of Breakthrough Pain

- Frequency: 1- 4 episodes per day
- Often unpredictable
  - Can be precipitated by action such as coughing or movement but can be spontaneous.
- Often significantly undertreated

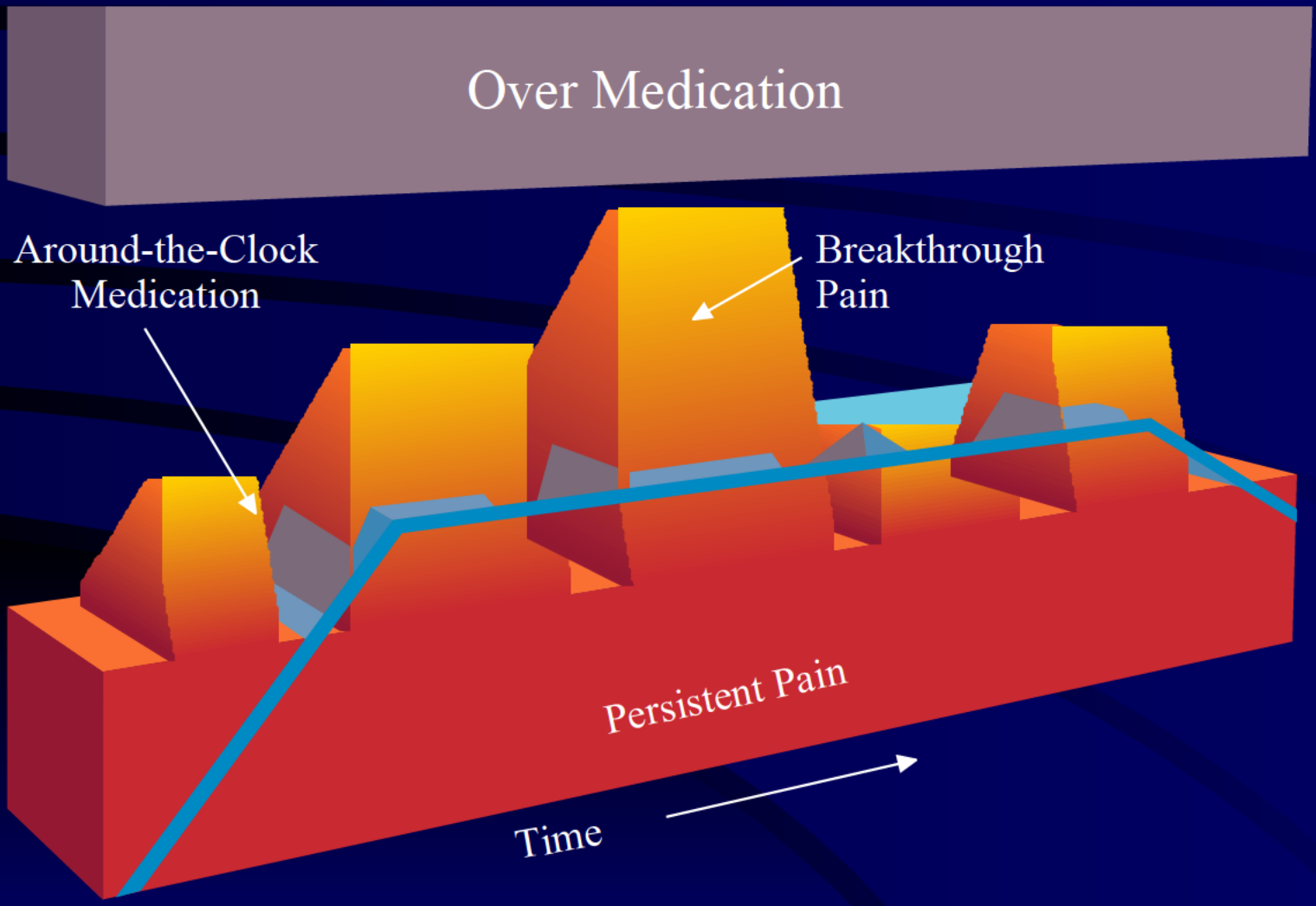
Terms Related to Breakthrough Pain

- Incident pain:
  - Occurs in relation to specific activities (i.e. walking, coughing)
- Idiopathic/spontaneous pain:
  - Occurs with no relationship to specific activities
- End-of-dose pain:
  - Occurs just prior to the next scheduled dose of a long-acting analgesic.

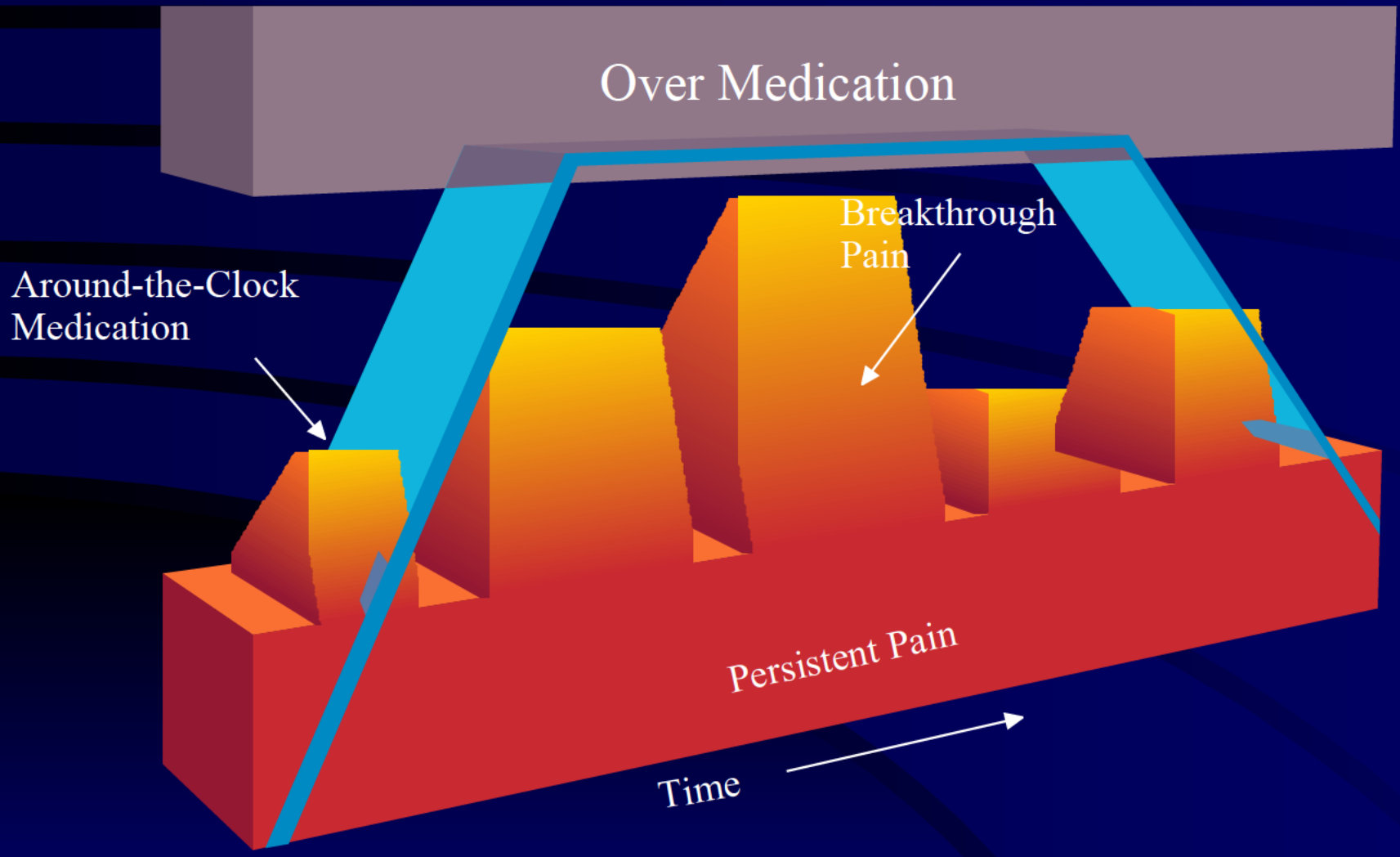
Treating Persistent Pain



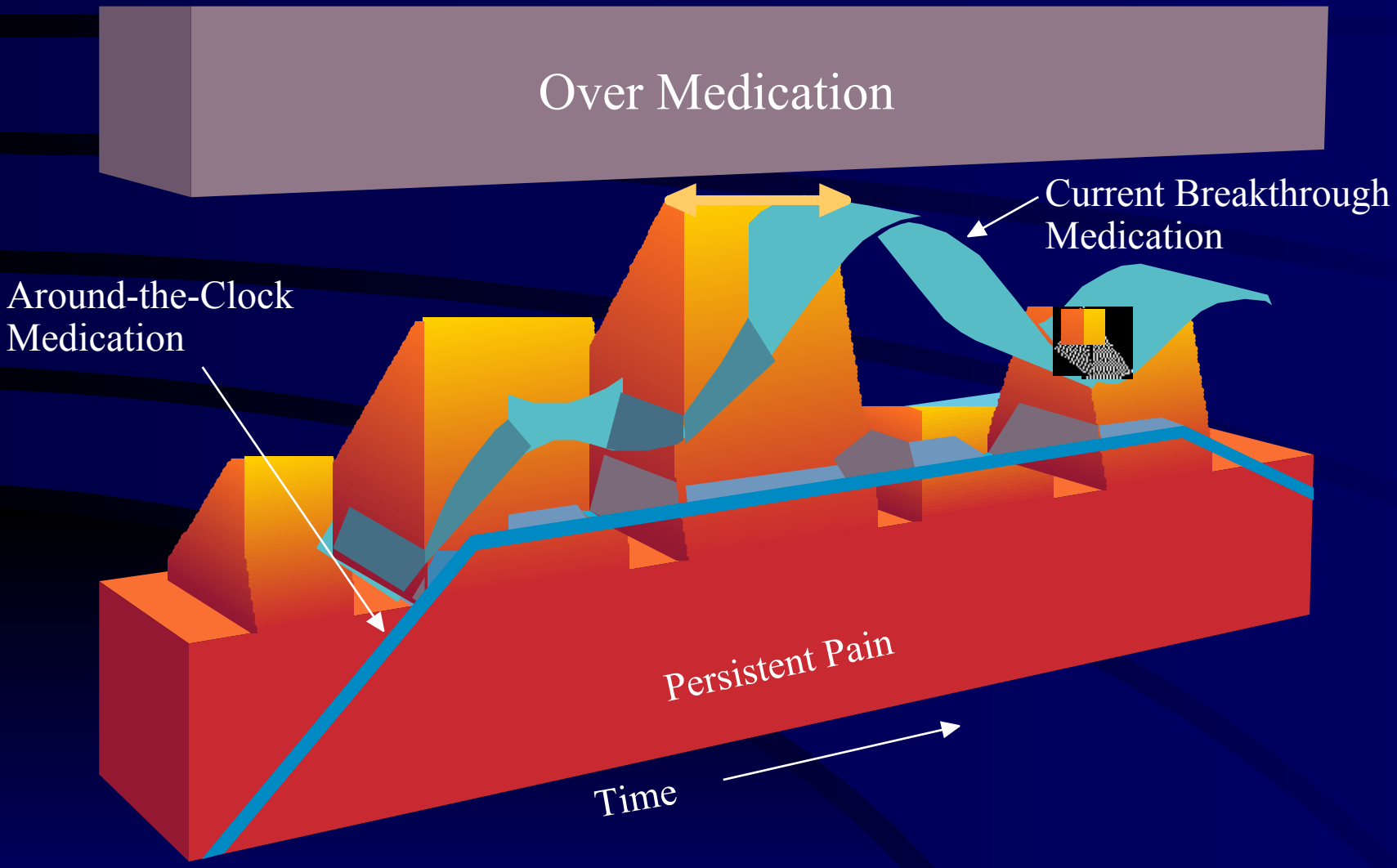
ATC Medications–Shortcomings



Increasing Dose of ATC Medication– More Side Effects



Treating Breakthrough Pain



Optimal Agent to Treat Breakthrough Pain

- Short-acting
- Easily administered
- Rapidly absorbed
- Readily titrated
- Should not overly sedate or cause adverse effects
- Strong enough to relieve severe pain
- Appropriate for frequent use
- Oral route preferred

Common Errors in Treating Breakthrough Pain

- Failure to recognize end-of-dose pain
- Treating BT with inadequate doses of analgesic
- Administering compound analgesics for BT
- Use of long-acting analgesics to treat BT
- Increasing basal analgesic doses instead of treating BT
- Inappropriate route of administration of analgesic

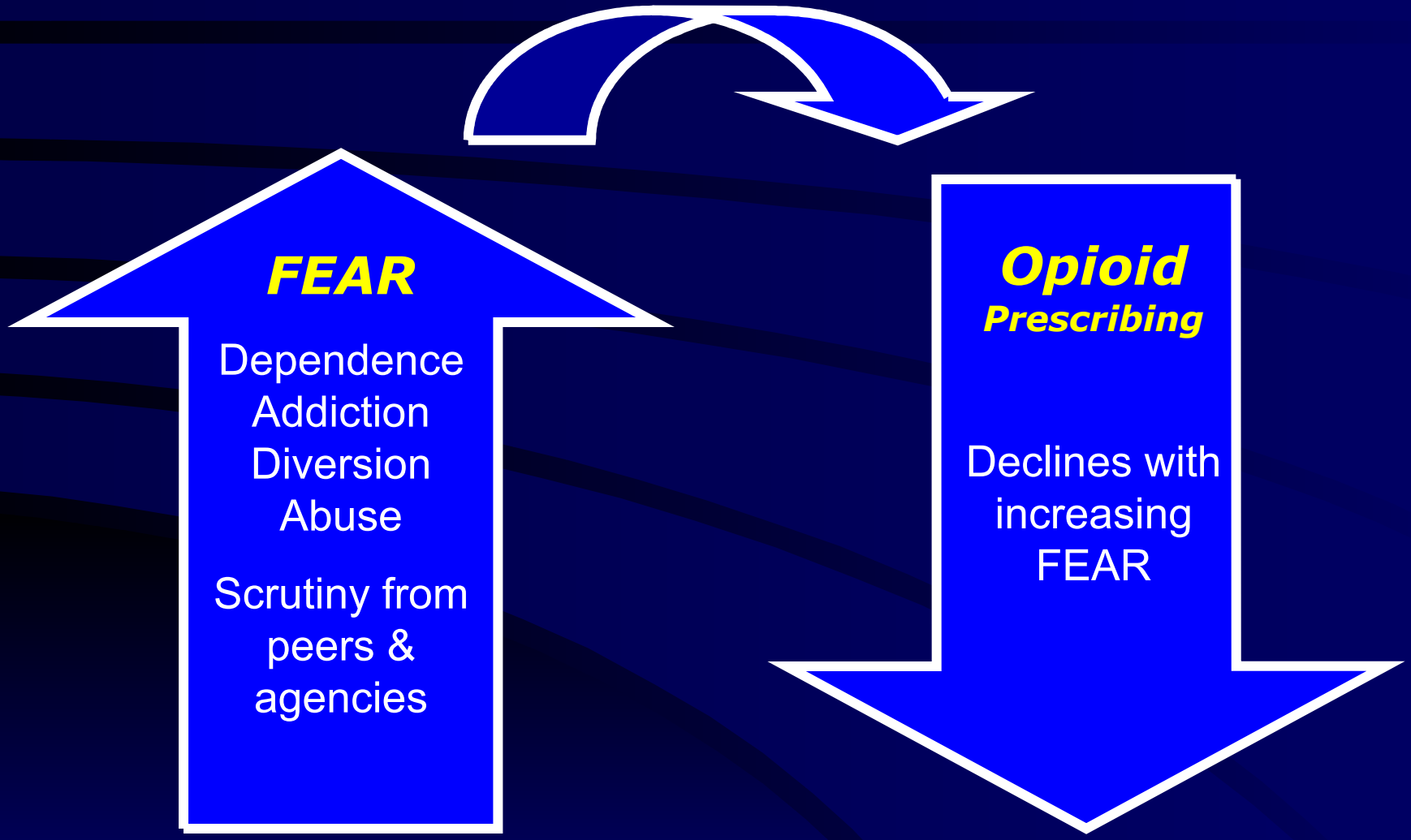
Prescription Drug Abuse

- Prescription drug abuse is a serious US public health problem
- 2002 National Survey of Drug Use and Health in ages 18-25
  - Prevalence of lifetime, non-medical pain reliever use
  - 6.8% (1992) to 19.4% (2001) to 22.1% (2002)
- 2003 National Institute Drug Abuse survey of 12th graders
  - non-medical use of medications
  - 10.5% used Vicodin
  - 4.5% used OxyContin

True or False?

- Any patient who is given narcotics for pain relief is at significant risk for addiction.
- When narcotics are used to control chronic pain, addiction is a common outcome.
- More than 5% of patients who receive narcotics for pain subsequently become addicts.
- Chronic pain of unknown cause should not be treated with narcotics even if this is the only way to obtain pain relief.
- Using narcotics to relieve pain of benign conditions is ill-advised.

Fear Inhibits Opioid Prescribing



Perspective on Regulatory Concerns

- Fear of sanctions may lead to undertreatment of pain
- No federal laws prohibit appropriate opioid use for analgesia
- Recently published model guidelines may help reverse trends
- Recent joint statement issued by DEA and 21 health care organizations

Joint Statement: DEA and Health Care Organizations

- Undertreatment of pain is a serious problem
- Effective pain management is an integral and important aspect of quality medical care
- Pain should be treated aggressively
- For many patients, opioids are the most effective treatment
  - Using established management guidelines
  - Often the only option that provides significant relief
- The balance comes from also recognizing the need to address abuse and diversion of opioids

Drug Enforcement Administration, DEA Press release, 10/23/01.

Drug Abuse

- Defining Drug Abuse
  - Intentional overuse in cases of celebration, anxiety, despair, self-medication, or ignorance
  - The use of medications outside the scope of usual medical practice
  - The use of illicit substances
- Abusers may or may not be addicts
- Abusers can often stop use when harmed

Based on the Diagnostic and Statistical Manual-IV (DSM-IV)

Addiction
Consensus Medical Definition

"A primary, chronic neurobiological disease with genetic, psychosocial and environmental factors influencing its development and manifestation"

AAPM, APS, ASAM. Definitions Related to the Use of Opioids for the Treatment of Pain. [consensus document] 2001.

Addictive Behaviors

Addictive behaviors include one of the following:

- Impaired control over drug use
- Compulsive use
- Continued use despite harm (physical, mental, and/or social)
- Craving

AAPM, APS, ASAM. Definitions Related to the Use of Opioids for the Treatment of Pain. [consensus document] 2001.

Chronic Use vs. Abuse

Addiction:

- Dysfunctional pattern of opioid use for purposes other than alleviating pain
- Loss of control over the use of opioids
- Preoccupation with obtaining opioids despite the presence of adequate analgesia
- Iatrogenic addiction is very rare.

Consequences of Addictive Use of Medications

- Persistent sedation or intoxication due to overuse
- Increasing functional impairment and other medical complications
- Psychological manifestations such as irritability, apathy, anxiety and/or depression

AAPM, APS, ASAM. Definitions Related to the Use of Opioids for the Treatment of Pain. [consensus document] 2001.

Pseudoaddiction

- Behaviors that may occur when pain is inadequately treated (severe, unrelieved pain)
- Patients may become focused on obtaining medications ("drug-seeking behavior")
- Behavior mimics addiction (hoarding)
- Focus is relief of pain
- Behaviors resolve when pain is appropriately treated

AAPM, APS, ASAM. Definitions Related to the Use of Opioids for the Treatment of Pain. [consensus document] 2001.

Physical Dependence

- Abstinence syndrome caused by dose reduction, abrupt discontinuation or administration of an antagonist
- Natural physiologic process
- Abstinence symptoms can often be avoided with careful tapering/monitoring for withdrawal symptoms
- May exist after few days of regular opioid dosing but onset is highly variable
- Does not independently cause or define addiction
- Should be made clear to patient and caregiver

AAPM, APS, ASAM. Definitions Related to the Use of Opioids for the Treatment of Pain. [consensus document] 2001.

Tolerance

- Escalating dose required to maintain the same effect
- May develop at different rates for different effects
  - Tolerance to sedation and nausea occur relatively rapidly
  - Tolerance to constipation may not occur at all
- Tolerance to analgesia is seldom a clinical problem
  - Tolerance rarely "drives" dose escalation
  - Tolerance does not cause addiction
- "Pseudotolerance": worsening disease leads to increased dose requirement

AAPM, APS, ASAM. Definitions Related to the Use of Opioids for the Treatment of Pain. [consensus document] 2001.

Diversion

- Diversion – The willful transfer of a drug from legitimate supply (manufacture, distribution, or storage in hospitals, pharmacies, physicians' offices) and/or patients for whom the drug has been prescribed to unauthorized users and/or for illegal sale
- Examples
  - Stolen, altered or forged prescriptions
  - Trading for profit on medication from others
  - Scams

Prevalence of Abuse

- Overall prevalence cited in some studies may not reflect real life statistics related to abuse / addiction
- Clear message is that pain itself is not an independent risk factor for abuse of pain medications
- The majority of legitimate pain patients do **not** abuse their analgesic medication

US Population Statistics

Addictive behavior occurs in a significant proportion of the population:

- 7.1 % use illicit drugs
  - 1.6% used prescription-type pain relievers non-medically
- 1.4% are dependent on or abuse illicit drugs
- 20.6% abuse alcohol (reported binge drinking)
- 29.5% use tobacco products

2001 National Household Survey on Drug Abuse. Substance Abuse and Mental Health Services Administration, 2002

Opioid Agreements

- Designed to facilitate
  - Informed consent about opioid risks and side effects
  - Patient education
  - Compliance
- Help describe the pain treatment plan
- Noncompliance may aid in diagnosis of addiction or substance abuse relapse
- Have the potential to improve therapeutic relationship
  - Must be based on mutual trust and honesty

Document the Four "A's"

- **A**nalgesia
- **A**ctivities of daily living
- **A**dverse events
- **A**berrant drug taking

Additional Types of Cancer-related Pain

- Diffuse bone pain
- Neuropathic pain
- Movement-related pain
- Mucositis

General Principles of Pain Management

- Individualize the pain regimen to the patient.
- Discuss pain and its management with the patient.
- Encourage the patient to participate.
- Reassure those reluctant to report pain.
- Consider the cost of therapy.

Common Causes of Analgesic Failure

- Overestimating the analgesic efficacy of a drug.
- Underestimating the analgesic requirements of the patient.
- Prejudice against the use of analgesics that may prevent objective therapy.
- Lack of knowledge of analgesic pharmacology.

Common Causes of Analgesic Failure

- Patient non-adherence because of fear of addiction.
- Patient not communicating with caregivers because of fear of being labeled a drug addict.
- Patient wants to please by not complaining.
- Patient does not know how to or is afraid to communicate with caregiver.

WHO Three-Step Pain Ladder

- Non-opioid
  - ± adjuvant
- Opioid for mild to moderate pain
  - + non-opioid
  - ± adjuvant
- Opioid for moderate to severe pain
  - ± non-opioid
  - ± adjuvant

Opioids for Mild–Moderate Pain

- Codeine
- Oxycodone (Percocet, Percodan)
- Meperidine (Demerol)
- Propoxyphene (Darvon, Darvocet)
- Hydrocodone (Vicodin, Lortab)
- Tramadol (Ultram)
- Pentazocine (Talwin, Talwin NX)

Opioids for Severe Pain

- Morphine
- Hydromorphone (Dilaudid)
- Oxycodone (OxyContin)
- Methadone
- Levorphanol (Levo-Dromoran)
- Fentanyl (Duragesic, Actiq)
- Oxymorphone (Numorphan)

Palliative Therapies

- Radiation Therapy
- Nerve blocks
- Surgery
- Antineoplastic Therapy
- Psychosocial interventions
- Physical modalities

General Types of Medications

- Nonopioid analgesics
- Opioid analgesics
  - Long-acting medications
  - Short-acting medications
- Analgesic adjuvants

Types of Opioids

- Full agonists
  - Morphine
- Mixed agonist-antagonists
  - Pentazocine (Talwin)
- Partial agonists
  - Buprenorphine (Buprenex)
- Centrally acting
  - Tramadol (Ultram)

Full Agonists

- Morphine
- Codeine
- Fentanyl
- Hydromorphone (Dilaudid)
- Meperidine (Demerol)
- Methadone
- Levorphanol (Levo-Dromoran)
- Oxycodone (OxyContin)
- Propoxyphene HCl (Darvon)
- Propoxyphene Napsylate (Darvon-N)
- Hydrocodone (Vicodin, Lortab)
- Oxymorphone (Numorphan)

Mixed Effects

Partial Agonists

- Buprenorphine (Buprenex)
- Dezocine (Dalgan)

Agonist/Antagonists

- Butorphanol (Stadol, Stadol NS)
- Nalbuphine HCl (Nubain)
- Pentazocine (Talwin, Talwin NX)

Opioid Receptors

- Mu (μ): 70% of total receptor population
  - Analgesia
  - Habituating and withdrawal effects
  - Central analgesia and respiratory depression
- Kappa (κ): 6% of total receptor population
  - Analgesia
- Delta (δ): 24% of total receptor population
  - Analgesia
  - May play a role in euphoria

Opioid Allergy

- Can cause pruritic rashes and other true allergic-type reactions
- Opioids stimulate histamine release from mast cells
- Can cause a local wheal, burning, itching and erythema at the site of injection
- Systemic release of histamine can cause localized or generalized flushing
- True opioid allergies are infrequent

Opioid Allergy

- **Phenanthrenes** (morphine, codeine, hydrocodone, hydromorphone, hydrocodeine, oxycodone, levorphanol, nalbuphine, butorphanol, dezocine, dihydrocodeine)
- **Phenylpiperidines** (meperidine, fentanyl, alfentanil, sufentanil)
- **Phenylheptanones** (methadone, propoxyphene)

Opioid Allergy

- Allergic reactions may cross-react within the same chemical class
- Less likely to react between structural classes
- Patients with “true” allergies can be switched with a product in one of the other classes.

Inhibitory Effects of Morphine

- Suppress pain
- Drowsiness, sedation
- Decreased respiration
- Increased intracranial pressure
- Suppress cough
- Decrease peristalsis
- Inhibit fluid and electrolyte accumulation in the lumen of the intestine
- Decrease gastric acid secretion
- Slight decrease in temp
- Decreased LH and FSH

Stimulatory Effects of Morphine

- Euphoria
- Constriction of pupils (miosis)
- Stimulation of the chemoreceptor trigger zone (CTZ)
- Increase intestinal smooth muscle tone
- Increase detrusor muscle tone
- Increased prolactin and antidiuretic hormone release
- Proconvulsant in overdose

Side Effects of Morphine in Cancer Patients

Titration:

- Nausea
- Vomiting
- Constipation
- Sedation
- Xerostomia
- Sweating
- Pruritus
- Respiratory depression

Maintenance:

- Constipation
- Sedation
- Xerostomia
- Hallucinations
- Hyperalgesia, allodynia
- Myoclonus
- Cognitive failure
- Respiratory depression

Guillermo V, et al. Cancer Nurs 1998;21(4):289-297.

Cherny N, et al. J Clin Onc 2001;19(9):2542-2554.

Morphine Metabolism

- Glucuronized in the liver and intestinal mucosa
- Three different metabolites
  - Morphine-3-glucuronide (M-3-G)
  - Morphine-6-glucuronide (M-6-G)
  - Normorphine

Morphine-6-Glucuronide

- Opioid binding agent with analgesic properties
- Higher affinity for the mu receptor than morphine
- Twice as potent as morphine when given systemically.
- One hundred times more potent when given intrathecally in animals.
- Accounts for a portion of morphine's analgesic effect

Morphine-6-Glucuronide

- With chronic dosing blood levels of M-6-G exceed morphine.
- Known to accumulate in renal failure
- May also accumulate in patients receiving codeine
- May be responsible for late opioid toxicity
- Develop progressive sedation, myosis, sweating and respiratory depression

Morphine-3-Glucuronide & Normorphine

M-3-G:

- Non-opioid binding agent
- Ability to cause generalized hyperexcitability, myoclonus and grand mal seizures

Normorphine:

- Capable of causing significant central hyperexcitability
- May cause hallucinations

Criteria for Drug Selection

- Oral administration is preferred
- Dosing interval (adherence issues)
- Adverse effects
- Potential drug interactions
- Concomitant illnesses

Long-Acting Preparations

- Morphine (MS Contin)
- Oxycodone (OxyContin)
- Hydromorphone (Palladone)
- Fentanyl (Duragesic)

Morphine Controlled Release

MS Contin Tablets

- Purdue Frederick
- 15mg, 30mg, 60mg, 100mg & 200mg
- Initial dose 15-30mg q8-12 hours
- Extent of absorption same as conventional oral morphine.

Morphine Controlled Release

MS Contin Tablets

- Only 40% of the administered dose reaches the central compartment
- Extent of absorption occurs, on average, after 1.5 hours, half-life 2-4 hours
- Fatty meal may cause a slight decrease in peak concentration

Morphine Controlled Release

MS Contin Tablets

- Does not release morphine continuously over the course of a dosing interval
- Will result in higher peaks and lower trough plasma levels when dosed q12 hours
- Tablets are to be taken whole, not crushed or chewed

Morphine Controlled Release

Oramorph SR Tablets

- Roxane Laboratories
- 15mg, 30,mg, 60mg & 100mg
- Initial dose 15-30mg q8-12 hours
- Extent of absorption same as conventional oral morphine.

Morphine Controlled Release

Oramorph SR Tablets

- Only 40% of the administered dose reaches the central compartment
- 50% of absorption occurs, on average, after 1.5 hours, time to peak 3.7 hours
- Half-life 2-4 hours

Morphine Controlled Release

Oramorph SR Tablets

- Does not release morphine continuously over the course of a dosing interval
- 90% of dose is metabolized
- M-3-G (55-75%), M-6-G (1-5%)
- Tablets are to be taken whole, not crushed or chewed

Morphine Sustained Release

Kadian Capsules

- Faulding Laboratories
- 20mg, 30mg, 50mg, 60mg, & 100mg
- Initial dose 20mg q12 hours or q24 hours
- Slower release than SR tablets
- T_{max}: Single dose 8.6 hours, Multiple dose q24 hours 10.3 hours

Morphine Sustained Release

Kadian Capsules

- 50% of absorption occurs, on average, after 8 hours
- Food slows the rate of absorption but not the extent
- Contraindicated in patients with paralytic ileus

Morphine Sustained Release

Kadian Capsules

- Increase dose no more than every other day
- Swallow capsules whole.
- Do not chew, crush or dissolve capsule
- May open capsule and sprinkle on apple sauce, room temperature or cooler

Morphine Extended Release

Avinza Capsules

- Ligand Pharmaceuticals
- First agent for q24 dosing only
- 30mg, 60mg, 90mg & 120mg
- Contains both immediate-release and extended-release beads
- Designed to maintain morphine plasma levels throughout the day.
- Initial dose 30mg q24 hours

Morphine Extended Release

Avinza Capsules

- Dose may be increased every 4 days
- Maximum daily dose 1600mg
- Capsules contain fumaric acid (FA) as an inactive ingredient.
- FA is an osmotic agent so fluid enters the bead to dissolve the drug
- The amount of FA in 1600mg is considered unsafe and may cause renal toxicity

Morphine Extended Release

Avinza Capsules

- Morphine blood levels may persist for 36 hours after discontinuation
- Less peak/trough fluctuations than SR tablets
- Swallow capsules whole.
- Do not chew, crush or dissolve capsule
- Capsules can be opened and sprinkled on apple sauce, room temperature or cooler

Oxycodone Controlled Release

OxyContin Tablets

- MISUSE, ABUSE & DIVERSION!
- Purdue Pharma L.P.
- 5mg, 10mg, 20mg, 40mg, 80mg & 160mg**
- Initial dose 10mg q12 hours
- Oral bioavailability 60-87%, low pre-systemic & first-pass metabolism
- Half life 4.5 hours, Tmax approximately 3 hours

**Voluntarily withdrawal 5/01

Oxycodone Controlled Release

OxyContin Tablets

- Steady state levels in 24-36 hours
- Exhibits a biphasic absorption pattern with the initial release of oxycodone from the tablet followed by a prolonged release
- A high-fat meal can increase plasma concentrations by 25%
- Not indicated for rectal administration due to increased AUC and peak levels

Oxycodone Controlled Release

OxyContin Tablets

- Metabolized to noroxycodone, oxymorphone and their glucuronides
- Noroxycodone is a considerably weaker analgesic then oxycodone
- Oxymorphone possesses analgesic activity but is present in only low plasma concentrations
- Formation of oxymorphone is mediated by CYP2D6

Oxycodone Controlled Release

OxyContin Tablets

- Females have a 25% higher oxycodone plasma concentration than males when adjusted for weight
- Tablets are to be taken whole, not crushed or chewed
- Empty “ghost” tablets may appear in the stool

Hydromorphone Extended Release

Palladone Capsules

- Purdue Pharma L.P.
- 12mg, 16mg, 24mg & 32 mg capsules
- Formulated for once daily dosing
- Initial dose: equivalent opioid conversion and then titrate every 2-3 days
- Oral absorption: Biphasic (2,16 hrs –less fluctuation vs. q6 hr dosing)
- Half-life: 18.6 hrs Tmax: 2 hrs

Hydromorphone Extended Release

- Indicated for patients who:
  - are already receiving opioid therapy
  - have demonstrated opioid tolerance (x1 week)
    - 60 mg oral morphine/day
    - 30 mg oral oxycodone/day
    - 8 mg oral hydromorphone/day
    - Any other equianalgesic dose of another opioid
  - require a minimum total daily dose of 12 mg of oral hydromorphone or opioid equivalent.

Hydromorphone Extended Release

- Pellet formulation which uses a controlled release melt extrusion technology.
- Each pellet contains the same amount of hydromorphone with different capsule fill weights used to vary strengths.
- Do not break, chew or open capsules.
- Alcohol can lead to a rapid release and absorption of a potentially fatal hydromorphone dose

Hydromorphone Extended Release

- An FDA required patient medication guide must be dispensed to all patients. The drug is:
  - one for which patient labeling could help prevent serious adverse effects.
  - one that has serious risks of which patients should be made aware because information concerning risks could affect the patient's decision to use or continue to use the drug.
  - important to health and patient adherence to directions for use is crucial to the drug's effectiveness.

Fentanyl Transdermal

Duragesic Patch

- Janssen Pharmaceuticals (Alza manufactures)
- 12.5 mcg/hr, 25mcg/hr, 50mcg/hr, 75mcg/hr & 100 mcg/hr
- Each patch lasts for 72 hours
- Initial dose 25mcg/hr patch q72 hours
- Small amount released with initial application

Fentanyl Transdermal

Duragesic Patch

- The rate of delivery to the skin may vary across the 72 hour application time
- The labeled strength represents the average quantity of fentanyl delivered to the systemic circulation per hour
- Absorption is subject to intra as well as intraindividual variability

Fentanyl Transdermal

Duragesic Patch

- Rate and extent of absorption may vary based on temperature, hydration and skin integrity
- 92% of the fentanyl in the patch is absorbed over 72 hours
- Some patients require q48 hour dosing
- Onset of action is very slow, 12-24 hours

Fentanyl Transdermal

Duragesic Patch

- Peak serum levels generally occur between 24-72 hours (approximately 36 hours)
- Primarily metabolized by CYP3A4
  - Be aware of CYP3A4 inducers and inhibitors
- Analgesic effect may last for several hours after patch is removed
- May use more than one patch based on pain control

Fentanyl Transdermal

Sandoz's Fentanyl Transdermal Patch

- Sandoz (Alza manufactures)
- Exactly the same as Duragesic, liquid reservoir.
- 25mcg/hr, 50mcg/hr, 75mcg/hr & 100 mcg/hr
- AB rated by FDA vs. Duragesic
- Patients have reported differences in analgesic efficacy and side effects.

Fentanyl Transdermal

Mylan's Fentanyl Transdermal Patch

- Mylan Pharmaceuticals
- 25mcg/hr, 50mcg/hr, 75mcg/hr & 100 mcg/hr
- AB rated by FDA vs. Duragesic
- Mylan's patch is smaller
- Utilizes a solid matrix fentanyl-containing silicone adhesive that is sandwiched between backing film and protective liner.

Short-acting Preparations

- Morphine (MSIR)
- Hydromorphone (Dilaudid)
- Oxycodone (OxyIR, OxyFAST)
- Oxycodone & acetaminophen (Percocet)
- Hydrocodone (Vicodin, Lortab)
- Methadone
- Propoxyphene
- Tramadol (Ultram)
- Fentanyl (Actiq)

Breakthrough Pain Management

- Ideal agent should be absorbed quickly
- Rapid onset of analgesic effect
- Strong enough to relieve pain
- Short acting
- No pharmacologic rationale to support the administration of any fixed ratio of rescue drug to baseline medication

P-kinetic Characteristics of Opioids

- The duration of analgesia of an opioid correlates partially with its:
  - Serum half-life
  - Dose
  - Route of administration
  - Distribution characteristics of the drug.

P-kinetic Characteristics of Opioids

- Methadone has a very long half-life of 24 hours, buts its duration of analgesia is only about 6 hours.
  - However, single daily doses are retained on opiate receptors in the brain long enough to satisfy the craving for opiates in addicts.
  - When given epidurally its duration of analgesia is extremely short due to its high lipophilicity and rapid distribution from the epidural space.

Morphine Oral Solution

- MSIR*, Roxanol** - 10mg/5mL
- MSIR, Roxanol - 20mg/5mL
- Roxanol UD 30mg/1.5mL
- MSIR, Roxanol, Roxanol T - 20mg/1mL
- Roxanol 100 - 100mg/5mL
  - Initial dose 10-30mg q4 hours

*Purdue Pharma

**Roxane

Morphine Tablets/Capsules

- MSIR* Tablets** 15mg, 30mg
- MSIR Capsules** 15mg, 30mg
- Morphine Soluble Tablets*** 10mg, 15mg, 30mg
  - Initial dose 10-30mg q4 hours

*Purdue Pharma

**Various Generics: Roxane, Ethex

***Ranbaxy (for dilution & injection)

Morphine Suppositories

- RMS*, Various generic brands**
  - 5mg
  - 10mg
  - 20mg
  - 30mg
- Initial dose 10-20mg q4 hours

*Upsher-Smith

**Paddock, Roxane

Immediate Release Morphine

- Onset: 30 min, 30-45 min*
- Bioavailability: 40% (variable)
- Peak Effect: 60 min, 60-120 min**
- Active Metabolites: Yes
- Distribution: Hydrophilic
- Duration: 4 hr, 4-6 hrs**

* AHFS 2005

** USPDI 2005

Hydromorphone

Tablets

- Dilaudid* 1mg, 2 mg, 3mg, 4mg, 8mg
- Generic** 2mg, 4mg, 8mg

Oral Liquid

- Dilaudid-5*, generic** 5mg/5mL

Suppositories

- Dilaudid* 3mg

* Knoll
** Roxane, Endo

Hydromorphone

Tablets

- Initial dose 2mg q4-6 hours

Oral Liquid

- Initial dose 2.5mg q4-6 hours

Suppositories

- Initial dose 3mg q6-8 hours

* Knoll
** Roxane, Endo

Hydromorphone Oral/Rectal

- Onset: 22 min, 30 min*,***, 15-30 min**
- Bioavailability: Well absorbed
- Peak Effect: 44 min, 90-120 min***
- Active Metabolites: No
- Distribution: Hydrophilic
- Duration: 4-6 hrs, 4-5 hrs**, Rectal 6-8 hrs

* Dilaudid Product Information

** AHFS 2005

*** USPDI 2005

Oxycodone

5 mg Tablets

- M-Oxy*, Percolone**, Roxicodone***, Endocodone** , Various generics****

Tablets, immediate-release

- Roxicodone*** 15mg, 30mg

Capsules, immediate-release

- OxyIR*****, Oxycodone HCl**** 5 mg

* Mallinckrodt

** Endo

*** Roxane

**** Amide, Ethix, Watson

***** Purdue Pharma

Oxycodone

Oral Solution

- Roxicodone*** 5mg/5mL

Concentrated Oral Solution 20mg/mL

- Roxicodone Intensol***, Oxy dose****, OxyFAST*****

*** Roxane

**** Amide, Ethix, Watson

***** Purdue Pharma

Oxycodone

5 mg Tablets

- Dose 2-6 tablets q4-6 hours prn

Tablets, immediate-release

- Dose 15-30mg q4-6 hours prn

Capsules, immediate-release

- Dose 5mg q6 hours prn

Oxycodone

Oral Solution 5mg/5mL

- Dose 10mg-30mg q4-6 hours prn

Concentrated Oral Solution 20mg/mL

- Dose 10mg-30mg q4-6 hours prn

Oxycodone

- Onset: 30 min, 10-15 min*
- Bioavailability: 60-87%
- Peak Effect: 60 min, 30-60 min**
- Active Metabolites: Noroxycodone, oxymorphone
- Distribution: Hydrophilic
- Duration: 4-6 hrs, 3-4 hrs**

* AHFS 2005

** USPDI 2005

Oxycodone & Acetaminophen

Percocet Tablets (Endo)

- 2.5mg oxycodone /325 APAP
- 5/325
- 7.5/325, 7.5/500
- 10/325, 10/650

- Dose 1-2 tablets q4-6 prn
- Maximum of 4gm of APAP per 24 hours

Oxycodone & Aspirin

Percodan Tablets (Endo)

- 4.5mg oxycodone HCl, 0.38mg oxycodone terephthalate, 325mg ASA
- 1 tablet q6 hrs prn

Percodan-Demi (Endo)

- 2.25mg oxycodone HCl, 0.19mg oxycodone terephthalate, 325mg ASA
- 1-2 tablets q6 hrs prn

Not to exceed 4 gm ASA daily

Methadone

Tablets 5mg, 10mg

- Roxane, Mallinckrodt, Eli Lilly

Oral Solution 5mg/5mL, 10mg/5mL

- Roxane

Oral Concentrate 10mg/1mL

- Roxane, Mallinckrodt

Usual Dosage 5-10mg q6-8 hrs prn

Methadone

- Onset: 30-60 min*
- Bioavailability: 80%** (41-99%)
- Peak Effect: 90-120 min*
- Active Metabolites: No
- Distribution: Lipophilic
- Duration: 4-6 hrs*

* USPDI 2005

** Mancini I, et al. Cur Opin Onc 2000;12:308-313

Meperidine (Demerol)

Many drawbacks

- 3 hour duration of action
- Higher risk of dependence
- More likely to cause seizures (Normeperidine)
- Avoid in elderly
- Avoid with impaired renal function
- Avoid with seizure disorders
- Many drug interactions:
  - SSRIs
  - MAOIs
  - Triptans
  - DHE

Hydrocodone & Acetaminophen

- Vicodin 5/500 (Knoll)
  - 1-2 tablets q4-6 hr prn (max 8 tabs/24hrs)
- Vicodin ES 7.5/750
  - 1 tablet q4-6 hr prn (max 5 tabs/24hrs)
- Vicodin HP 10/660
  - 1 tablet q4-6 hr prn (max 6 tabs/24hrs)

Vicoprofen 7.5/200 Hydrocodone & **Ibuprofen**

- 1 tablet q4-6 hr prn

Hydrocodone & Acetaminophen

- Lortab (UCB Pharma Inc.)
  - 2.5/500, 5/500, 7.5/500, 10/500
- Lorcet HD (Forest Pharmaceuticals)
  - 5/500
- Lorcet Plus
  - 7.5/650
- Lorcet 10/650

Hydrocodone & Acetaminophen

- Ceta-Plus (Seatrace)
- Duocet (Mason)
- Hydrocet (Carnrick)
- Hydrogesic (Edwards)
- Anexsia (Mallinckrodt)
- Norco (Watson)
- Zydone (Endo)
- Alor (Atley)
- Azdone (Central)
- Damason-P (Mason)
- Panasal (EC Robins)

Propoxyphene (Darvon)

- Weak analgesic
- Many preparations combined with a nonnarcotic (Darvocet)
- Potentially toxic metabolite (Norpropoxyphene)
- Avoid in the elderly
- May be cardiotoxic

Tramadol (Ultram)

- Not recommended for cancer pain
- Dual mechanism of action
  - Mu receptor agonist
  - Serotonin and norepinephrine reuptake inhibitor
- Ceiling effect
- Max dose 400 mg per day
- Risk of seizures with excessive doses
- Drug interactions

Codeine

- Weak analgesic
- Doses over 65mg may produce decreased incremental analgesia
- More constipation and dysphoria then morphine
- Combined with ASA or APAP
- Four hour duration of action
- 10% metabolized to morphine

Fentanyl Transmucosal (Actiq)

- Onset: 15 min, 5-10 min
- Bioavailability: 50%
- Peak Effect: 20 min, 22 min, 15 min
- Active Metabolites: No
- Distribution: Lipophilic
- Duration: 1-3 hrs, 2-5 hrs, 25-30 min

Common Adjunctive Agents

- NSAIDs
- Steroids
- Anticonvulsants
- Antihistamines
- Antidepressants
- Benzodiazepines
- Stimulants
- Phenothiazines
- Clonidine
- Bisphosphonates

NSAIDs

- Effective for the relief of mild to moderate pain
- Musculoskeletal pain
- Very effective for bony neoplastic metastasis
- Opioid sparing effects
- APAP has no antiinflammatory effects

NSAIDs

- When pain relief is not attained with one NSAID then another should be tried
- No NSAID has been shown to be superior to any other
- Do not use with thrombocytopenia
- Gastrointestinal side effects
- Renal effects
- Frequently overlooked in pain management

Steroids

- Provide a range of effects
- Antiinflammatory
- Antiemetic
- Euphoric effects
- Appetite stimulation

Steroids

- Reduce cerebral and spinal cord edema
- Important in the management of spinal cord compression or elevated intracranial pressure
- Dexamethasone 16mg/day or equivalent
- Dexamethasone 10mg PO q6h
- Adverse effects: gastrointestinal bleeding, Cushing's syndrome, increased blood sugar.

Anticonvulsants

- Used to manage neuropathic pain
  - Gabapentin (Neurontin) 2400-3600mg/day
  - Phenytoin (Dilantin) 300mg/day
  - Carbamazepine (Tegretol) 600-1600mg/day
  - Valproate (Depakene, Depakote) 750-2250mg/day

Antihistamines

- Hydroxyzine (Vistaril)
  - 25-50mg PO/IM q4-6 hrs prn
- Mild analgesic properties?
- Predominantly utilized for its
  - Antiemetic effects
  - Anxiolytic effects
  - Sedating effects

Antidepressants

- Useful for neuropathic pain
- May potentiate opioid analgesia
- Amitriptyline (Elavil) 30-300mg daily
- Desipramine (Norpramin) 10-25mg qHS
- Sedating
- Anticholinergic side effects

Benzodiazepines

- Diazepam (Valium), lorazepam (Ativan)
- Treatment of acute anxiety
- Treatment of muscle spasm
- Not effective analgesics
- Respiratory depressant effects may limit opioid use

Stimulants

- May be useful in reducing opioid-induced sedation
- Methylphenidate (Ritalin) 5mg BID
- Dextroamphetamine (Dexedrine) 5mg BID
- Higher doses sometimes needed

Phenothiazines

- Pain complicated by delirium or nausea
- Fluphenazine (Prolixin)
  - 2mg PO q8 hrs
- Chlorpromazine (Thorazine)
  - 10-25mg PO/IM q4-6 hrs prn
- Prochlorperazine (Compazine)
  - 10mg PO/IM q6 hr prn

Bisphosphonates

- Pamidronate (Aredia)
- Alendronate (Fosamax)
- Reduce bone pain
- Hypercalcemia of malignancy (Aredia)

Clonidine

- Clonidine (Catapres)
- $Alpha_2$ receptor agonist
- Approved for use via epidural route
- Hypotension and bradycardia

Prialt (Ziconotide Intrathecal Inj.)

- FDA Approved 12/28/04
- **NOT AN OPIATE** (1st in a new class)
- Synthetic equivalent of a natural peptide found in the poisonous venom of the tiny cone snail (Conus magus)
- 1,000 times more effective in relieving pain than morphine without addictive potential

Prialt (Ziconotide Intrathecal Inj.)

- Binds to N-type calcium channels located in the spinal cord.
- Blocks N-type calcium channels.
- These channels facilitate passage of electrical signals from one nerve to another and up the spinal cord to the brain.
- If the channel is blocked the pain signal does not reach the brain.

Prialt (Ziconotide Intrathecal Inj.)

- Not available orally
- Used in patients refractory to opiates
- Needs IT infusion pump
- Psych symptoms and neuro impairment may occur during therapy
- Risk of infection due to IT route
- Must taper opiates because ziconotide does not interact with opiate receptors